Gastrointestinal Stromal Tumor Presenting as Perforated Diverticulitis

Jin K. Kim, MD, Sarah B. Bryczkowski, MD, Stephen G. Pereira, MD, Adam Rosenstock, MD, Ruifang Zheng, MD, Osvaldo Zumba, MD, George Mazpule, MD

Department of Surgery, Rutgers New Jersey Medical School, Newark, New Jersey, USA (Dr. Kim)

Department of Surgery, Hackensack Meridian Health JFK Medical Center, Edison, New Jersey, USA (Dr. Bryczkowski)

Department of Surgery, Hackensack University Medical Center, Hackensack, New Jersey, USA (Drs Pereira, Rosenstock, Zumba, Mazpule)

Department of Pathology, Rutgers New Jersey Medical School, Newark, New Jersey, USA (Dr. Zheng)

ABSTRACT

Introduction: Colonic gastrointestinal stromal tumors are rare and never have been reported to present as diverticulitis.

Case Description: We describe a case of a 63-year-old female who was treated for a perforated sigmoid diverticulitis which was secondary to a gastrointestinal stromal tumor.

Conclusion: While most major guidelines suggest treatment with adjuvant imatinib for intermediate or high risk gastrointestinal stromal tumors, there are discrepancies among the guidelines on the management of perforated tumors which warrant further studies to manage these patients.

Key Words: Gastrointestinal stromal tumor; Perforated GIST; Perforated diverticulitis.

Citation Kim JK, Bryczkowski SB, Pereira SG, Rosenstock A, Zheng R, Zumba O, Mazpule G. Gastrointestinal stromal tumor presenting as perforated diverticulitis. CRSLS e2019.00034. DOI: 10.4293/CRSLS.2019.00034.

Disclosures: none.

Conflicts of Interest: The authors have no conflicts of interest directly relevant to the content of this article.

Informed consent: Dr. Kim declares that written informed consent was obtained from the patient/s for publication of this study/report and any accompanying images.

Address correspondence to: Jin K. Kim, MD, 185 South Orange Ave G506, Newark, NJ 07103 USA. Phone: 973-972-4417, Fax: 973-972-6591, E-mail: jinjk1004@gmail.com

INTRODUCTION

Gastrointestinal stromal tumors (GISTs), which arise from the interstitial cells of Cajal, are the most common mesenchymal tumors of the gastrointestinal tract.[1] In adults, GISTs are frequently found in the stomach (60%) and small bowel (30%); GISTs in the colorectum (<5%) are rare.[2–4] Colonic GISTs typically present in the sigmoid colon with signs of bleeding or obstruction, and have the worst prognosis as they often present with high risk features.[2,5] In the United States, patients diagnosed with colonic GIST are predominately Caucasian with a mean age of 65 years, and there appears to be no gender predominance.[5] Here we report the first case of colonic GIST that presented as a perforated diverticulitis in a 63-year-old female and discuss risk stratification and management.

CASE PRESENTATION

A 63-year-old female with a history of hypertension and uterine fibroids status post myomectomy, presented with 1 day of acute-onset, severe right-sided abdominal pain associated with nausea, vomiting, and fevers. She reported undergoing an unremarkable colonoscopy 6 years ago. On examination, she was hemodynamically stable, and her abdomen was nondistended, soft, but with diffuse tenderness. Further workup revealed a leukocytosis of 12.5 $\times$ 10^9/L and a lactate of 3.3 mmol/L. After appropriate fluid resuscitation, her lac-

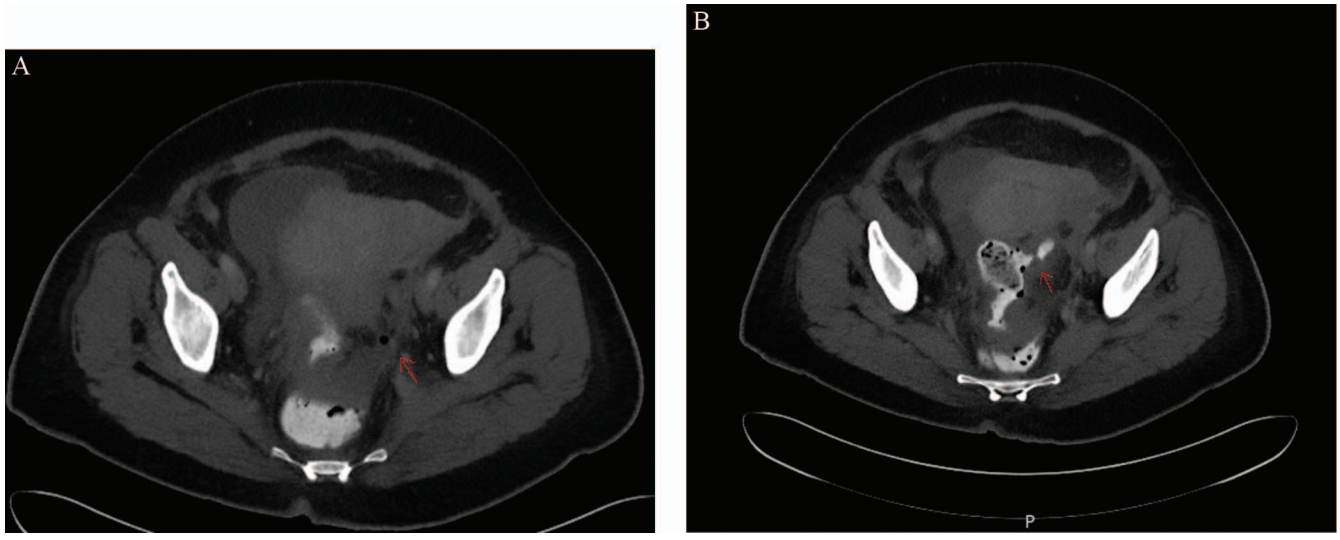

Figure 1. CT evidence of perforated sigmoid diverticulitis. Findings: perforated sigmoid diverticulitis, with increased inflammatory stranding and fluid in the abdomen and pelvis. **A**, Small amounts of extraluminal air (arrow). **B**, There is a 4-cm sigmoid diverticulum (arrow).

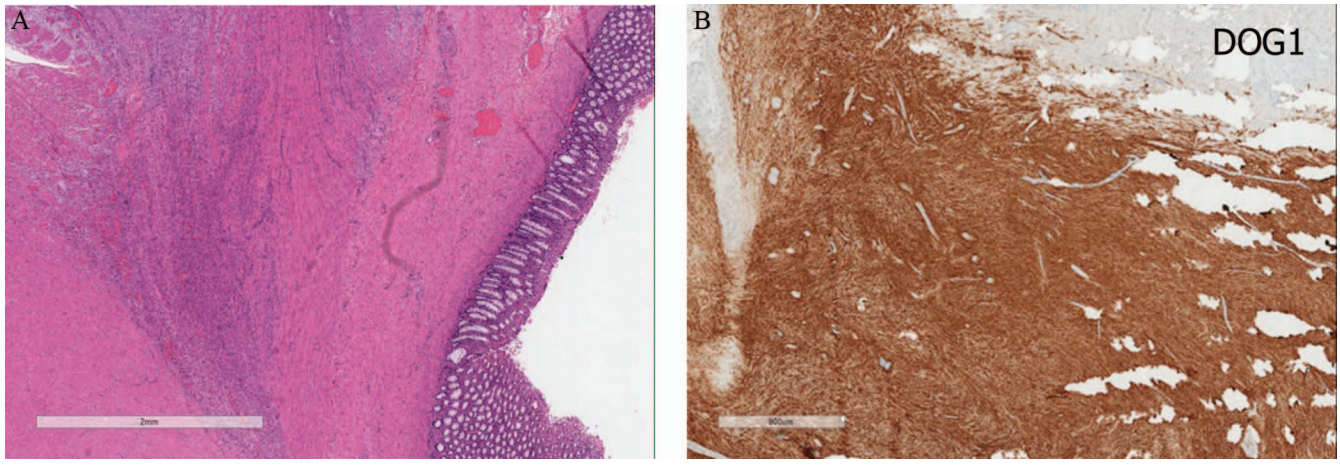

Figure 2. Pathologic Diagnosis of GIST. Findings: **A**, GIST developed in the muscularis propria of the large intestine. **B**, stained positive for DOG1.

tate trended down to normal limits. Our patient's Computed Tomography (CT) at both initial presentation and on hospital day 3 revealed a small pneumoperitoneum secondary to perforated sigmoid diverticulitis but no drainable abscess (**Figure 1, A** and **B**). The patient was initially treated with bowel rest and broad spectrum IV antibiotics (Piperacillin/Tazobactam); however, on hospital day 6, she was taken for diagnostic laparoscopy for persistent leukocytosis and abdominal tenderness. Laparoscopy revealed a small perforation in the medial portion of the sigmoid colon. Laparoscopic lavage and drain placement were done to address the intra-abdominal purulent abscess, and she was discharged home when stable.

The patient presented again about 1 month after discharge with recurrent fevers and peritonitis. Workup revealed a recurrent 8.2 × 3.2-cm intra-abdominal abscess, so the patient was taken back for repeat diagnostic laparoscopy, drain placement for the purulent abscess, and intravenous antibiotic treatment, which resolved her symptoms.

Several weeks after her second discharge, she underwent a colonoscopy, which revealed one polyp and sigmoid diverticulosis. She underwent an elective lapa-

Table 1.
Prognostic Tools of GIST: NIH Criteria

Risk Category	Tumor Size (cm)	Mitotic Count (per 50 HPF)
Very Low	<2	<5
Low	2–5	<5
Intermediate	<5	6–10
	5–10	<5
High	>5	>5
	>10	Any
	Any	>10

NIH, National Institutes of Health; HPF, High Power Field; GIST, Gastrointestinal stromal tumors.

Adapted from Fletcher et al.[7]

roscopic, robot-assisted sigmoid colectomy with an intent to treat her diverticular disease 3 months after initial presentation. Surprisingly, her pathology returned as 3.5-cm GIST in the muscularis propria of the pseudodiverticulum (**Figure 2A**) with mitotic rate of 1/50 High Power Field (HPF). Immunohistochemistry positive for CD 117, CD 34, DOG1 (**Figure 2B**). Lymph nodes were negative (0/10), and resection margins were negative.

DISCUSSION

GISTs are the most common mesenchymal tumors in the digestive tract and are commonly due to activating mutations in tyrosine kinase receptor KIT (CD 117) or platelet-derived growth factor receptor alpha.[3] Morphologically, GISTs appear as epithelioid and/or spindle-cell-like, which makes this disease particularly difficult to distinguish from other mesenchymal lesions such as schwannoma, leiomyoma, or leiomyosarcoma. While other mesenchymal lesions can also stain positive for CD 34, smooth muscle actin, and desmin (which are markers of GIST), GIST can be distinguished by positive CD 117 and/or DOG1 staining.[3,6] Of note, other tumors such as angiosarcoma and Ewing's sarcoma may also stain positive for CD 117; however, their morphology will appear different. Therefore the diagnosis of GIST relies on the concordance of both morphology and immunostaining.[3]

Several prognostic tools have been developed to stratify GIST into low, intermediate, and high risk for disease progression using variables that expanded over time[7] **(Tables 1–3)**. The well-known National Institutes of Health criteria, which was followed in early clinical trials supporting adjuvant imatinib, utilizes only tumor size and mitotic count to stratify recurrence risk.[7,8] The more recent American Forces Institute of Pathology criteria also considers tumor location, which is thought to improve prognostication.[7,9] The Joensuu criteria includes variables in the American Forces Institute of Pathology criteria and also characterizes tumor rupture as high risk.[10] These tools, while helpful in identifying more aggressive GISTs, are derived from retrospective data and have limitations. A prospectively validated nomogram that predicts recurrence-free survival based on the tumor size, mitotic index, and location is a useful adjunctive clinical tool.[11] Tumor rupture, however, has not yet been prospec-

Table 2.
Prognostic Tools of GIST: AFIP Criteria

Group	Tumor Parameters		Risk for Metastasis Based on Location of Primary GIST			
	Tumor Size (cm)	Mitotic Count (per 50 HPF)	Gastric	Jejunal and Ileum	Duodenum	Rectum
1	≤2	≤5	None	None	None	None
2	>2 to ≤5	≤5	Very low	Low	Low	Low
3a	>5 to ≤10	≤5	Low	Moderate	High	High
3b	>10	≤5	Moderate	High		
4	≤2	>5	NA	NA	NA	High
5	>2 to ≤5	>5	Moderate	High	High	High
6a	>5 to ≤10	>5	High	High	NA	NA
6b	>10	>5	High	High	High	High

HPF, High Power Field; AFIP, American Forces Institute of Pathology; GIST, Gastrointestinal stromal tumors.

Adapted from Miettinen et al.[8]

Table 3.
Prognostic Tools of GIST: Joensuu Criteria

Risk Category	Tumor Size (cm)	Mitotic Count (per 50 HPF)	Primary Tumor Site
Very low	≤2	≤5	Any
Low	>2 to ≤5	≤5	Any
Intermediate	>2 to ≤5	>5	Gastric
	<5	6–10	Any
	>5 to ≤10	≤5	Gastric
High	Any	Any	Tumor Rupture
	>10	Any	Any
	Any	>10	Any
	>5	>5	Any
	>2 to ≤5	>5	Nongastric
	>5 to ≤10	≤5	Nongastric

HPF, High Power Field; GIST, Gastrointestinal stromal tumors.
Adapted from Joensuu et al.[9]

tively validated to be a high-risk feature so it is unclear how to stratify these patients.

In terms of management, surgical resection with negative margins is often adequate for a localized GIST. However, many intermediate and high-risk GISTs metastasize most frequently in the liver or peritoneum.[1] Recent addition of tyrosine kinase inhibitor imatinib has shown to prolong recurrence free survival for CD 117–positive GISTs larger than 3 cm.[12–14] Currently, the National Comprehensive Cancer Network recommends adjuvant imatinib for 36 months to be considered in management of intermediate- or high-risk GIST patients.[3,12,14]

In our case, the patient's tumor size was small (3.5 cm) and mitotic count was low (1/50 HPF) which would classify it as low risk by both National Institutes of Health and American Forces Institute of Pathology criteria. However, because she presented with perforated diverticulitis with pathology showing GIST in the pseudodiverticulum, it was unclear whether to consider the tumor as ruptured since the Joensuu criteria would have categorized her disease as high risk if she did have tumor rupture. The patient's case was presented and discussed in a multidisciplinary meeting. Given that the risk of rupture in this case was theoretical and because the studies that describe tumor rupture as a risk factor involve patients with larger tumors with gross tumor rupture rather than microscopic perforations, the decision was ultimately made to treat as a low-risk GIST, and we opted for close observation with follow up at 3 months and yearly Computed Tomography (CT).

References:

1. Stamatakos M, Douzinas E, Stefanaki C, et al. Gastrointestinal stromal tumor. *World J Surg Oncol.* 2009;7:61.

2. Feng F, Tian Y, Liu Z, et al. Clinicopathological features and prognosis of colonic gastrointestinal stromal tumors: evaluation of a pooled case series. *Oncotarget.* 2016;7:40735–45.

3. Demetri GD, von Mehren M, Antonescu CR, et al. NCCN Task Force report: update on the management of patients with gastrointestinal stromal tumors. *J Natl Compr Canc Netw.* 2010; 8(Suppl 2):S1–S41; quiz S42–S44.

4. McDonnell MJ, Punnoose S, Viswanath YKS, Wadd NJ, Dhar A. Gastrointestinal stromal tumours (GISTs): an insight into clinical practice with review of literature. *Frontline Gastroenterol.* 2017;8:19–25.

5. Liu Z, Sun Y, Li Y, et al. Colonic gastrointestinal stromal tumor: a population-based analysis of incidence and survival. *Gastroenterol Res Pract.* 2019;2019:3849850.

6. Miettinen M, Lasota J. Gastrointestinal stromal tumors: review on morphology, molecular pathology, prognosis, and differential diagnosis. *Arch Pathol Lab Med.* 2006;130:1466–78.

7. Jones RL. Practical aspects of risk assessment in gastrointestinal stromal tumors. *J Gastrointest Cancer.* 2014;4:262–7.

8. Fletcher CD, Berman JJ, Corless C, et al. Diagnosis of gastrointestinal stromal tumors: a consensus approach. *Hum Pathol.* 2002;33:459–65.

9. Miettinen M, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. *Semin Diagn Pathol.* 2006;23:70–83.

10. Joensuu H. Risk stratification of patients diagnosed with gastrointestinal stromal tumor. *Hum Pathol.* 2008;39:1411–9.

11. Gold JS, Gönen M, Gutiérrez A, et al. Development and validation of a prognostic nomogram for recurrence-free survival after complete surgical resection of localised primary gastrointestinal stromal tumour: a retrospective analysis. *Lancet Oncol.* 2009;10:1045–52.

12. Balachandran VP, DeMatteo RP. Gastrointestinal stromal tumors: who should get imatinib and for how long? *Adv Surg.* 2014;48:165–83.

13. Demetri GD, Benjamin RS, Blanke CD, et al. NCCN Task Force report: management of patients with gastrointestinal stromal tumor (GIST)—Update of the NCCN clinical practice guidelines. *J Natl Compr Canc Netw.* 2007;5(Suppl 2):S1–S29; quiz S30.

14. Lim KT, Tan KY. Current research and treatment for gastrointestinal stromal tumors. *World J Gastroenterol.* 2017;23:4856–66.